PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT/03-11	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US04/11830	International filing date *(day/month/year)* 16 April 2004 (16.04.2004)	Priority date *(day/month/year)* 18 April 2003 (18.04.2003)
International Patent Classification (IPC) or national classification and IPC IPC: **C12Q 1/68**(2006.01),**C12P 3/00,C12N 9/02,C12N 1/13;C07H 21/04**(2006.01) USPC: 435/189,6,168,257.2;536/23.2		
Applicant MIDWEST RESEARCH INSTITUTE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03 February 2005 (03.02.2005)	20 June 2007 (20.06.2007)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Ponnathapu Achutamurthy Telephone No. 571-272-1600

Janice Ford for

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US04/11830

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-27 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 28 and 29 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1-6 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US04/11830

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 4-18

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4-18

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☒ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Please See Continuation Sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-3

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims NONE	YES
	Claims 1-3	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-3	NO
Industrial Applicability (IA)	Claims 1-3	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-3 lack novelty under PCT Article 33(2) as being anticipated by Dillon et al. (PGPUB US 2004/0209256 A1, publication 10/21/2004, claim priority of US copending application 10/411,910 filed on 4/12/2003). Dillon et al. teach an oxygen-tolerant or resistant iron hydrogenase, which can produce hydrogen in presence of oxygen. Dillon et al. also teach fragments or variants of hydrogenase, which are made by substitution of one or more amino acid residues preferably at amino acid positions in and near active site of hydrogenase resulting in oxygen tolerant or resistant hydrogenase. The mutants or variants of Dillon et al. inherently posses the mutation/substitution at the recited position of the instant application of claim 2 (see p1 col. 1-2).
Since the Office does not have the facilities for examining and comparing applicants' modified protein with mutations at specific positions with the the mutant orvariant protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed modified product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claims 1-3 meets the criteria set out in PCT Article 33(4), and thus meets industrial applicability because the subject matter claimed can be made or used in industry.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

IV. 3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is not complied with for the following reasons:

Group, I claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 78 of HydA1 iron hydrogenase.

Group, II claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 240 of HydA1 iron hydrogenase.

Group, III claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 244 of HydA1 iron hydrogenase.

Group, IV claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 86 of HydA1 iron hydrogenase.

Group, V claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 248 of HydA1 iron hydrogenase.

Group, VI claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 247 of HydA1 iron hydrogenase.

Group, VII claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 82 of HydA1 iron hydrogenase.

Group, VIII claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 89 of HydA1 iron hydrogenase.

Group, IX claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 355 of HydA1 iron hydrogenase.

Group, X claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 93 of HydA1 iron hydrogenase.

Group, XI claim(s) 1-3, drawn to an oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 252 of HydA1 iron hydrogenase.

Group, XII claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 78 of HydA1 iron hydrogenase.

Group, XIII claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 240 of HydA1 iron hydrogenase.

Group, XIV claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 244 of HydA1 iron hydrogenase.

Group, XV claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 86 of HydA1 iron hydrogenase.

Group, XVI claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 248 of HydA1 iron hydrogenase.

Group, XVII claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 247 of HydA1 iron hydrogenase.

Group, XVIII claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 82 of HydA1 iron hydrogenase.

Group, XIX claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 89 of HydA1 iron hydrogenase.

Group, XX claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 355 of HydA1 iron hydrogenase.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Group, XXI claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 93 of HydA1 iron hydrogenase.
Group, XXII claim(s) 4-7, drawn to a polynucleotide encoding oxygen-resistant iron hydrogenase polypeptide derived from oxygen-sensitive iron hydrogenase by substitution at position 252 of HydA1 iron hydrogenase.
Group, XXIII claim(s) 8-9 and 13, drawn to a method of producing hydrogen in green algae.
Group, XXIV claim(s) 10-12, drawn to a method of making nucleic acid encoding an oxygen-resistant iron hydrogenase.
Group, XXV claim(s) 14-18, drawn to a method of making an oxygen-resistant iron-hydrogenase.